

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the application.

IN THE CLAIMS:

1. (Currently Amended) A chemically modified nucleic acid molecule, wherein:
 - a. the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;
 - b. each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - c. an 18 to 27 nucleotide sequence of the antisense strand ~~of said nucleic acid molecule~~ is complementary to a human cholinergic receptor muscarinic 3 (CHRM3) RNA sequence comprising SEQ ID NO:305;
 - d. an 18 to 27 nucleotide sequence of the sense strand ~~of the nucleic acid molecule~~ is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human CHRM3 RNA sequence;
 - e. ~~about 50 to 100 percent or more of the nucleotides in the sense each strand and about 50 to 100 percent of the nucleotides in the antisense strand are chemically modified with modifications independently selected from the group consisting of 2' O methyl, 2'-deoxy 2' fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and~~
 - f. ~~one or more any of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2' O methyl purine nucleotides and one or more are differentially modified at a 2'-sugar position from any of the pyrimidine nucleotides at a 2'-sugar position present in one or both strands of the nucleic acid molecule are 2'-deoxy 2' fluoro pyrimidine nucleotides.~~

2.- 13. (Canceled)

14. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the purine nucleotides present in the sense strand are 2'-deoxy purine nucleotides.
15. (Canceled)
16. (Previously Presented) The nucleic acid molecule of claim 1, wherein the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends.
17. (Previously Presented) The nucleic acid molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.
18. (Canceled)
19. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides.
20. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the purine nucleotides present in said antisense strand are 2'-deoxy purine nucleotides.
21. (Currently Amended) The nucleic acid molecule of claim 1, wherein the antisense strand includes a ~~terminal~~ phosphorothioate internucleotide linkage at the 3'-end.
- 22.-29. (Canceled)
30. (Previously Presented) The nucleic acid molecule of claim 1, wherein the 5'-end of the antisense strand includes a terminal phosphate group.
31. (Previously Presented) A composition comprising the nucleic acid molecule of claim 1 in a pharmaceutically acceptable carrier or diluent.
32. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides.

33. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the pyrimidine nucleotides present in said sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
34. (Currently amended) The nucleic acid molecule of claim 1, wherein ~~1,2,3,4,5,6,7,8,9,10~~ or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
35. (Previously presented) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises one or more ribonucleotides.
36. (Previously presented) The nucleic acid molecule of claim 1, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides.
37. (Previously Presented) The nucleic acid molecule of claim 1, wherein the antisense strand, sense strand, or both the antisense strand and sense strand include a 3'-overhang of 1-3 nucleotides.
38. (Previously Presented) The nucleic acid molecule of claim 37, wherein the nucleotides of the 3'-overhang are chemically modified to comprise one or more phosphorothioate internucleotide linkages, 2'-O-methyl ribonucleotides, 2'-deoxy-2'-fluoro ribonucleotides, 2'-deoxy ribonucleotides, universal base nucleotides, 5-C-methyl nucleotides, inverted deoxyabasic moieties, or a combination thereof.
39. (Currently Amended) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule ~~further~~ includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more phosphorothioate internucleotide linkages in the sense strand, the antisense strand, or both the sense strand and the antisense strand.
40. (Currently Amended) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule ~~further~~ includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more 2'-O-methoxyethyl (MOE) nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.
41. (Currently Amended) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule ~~further~~ includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more locked nucleic acid (LNA)

nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.

42. (Currently amended) A chemically modified nucleic acid molecule comprising a sense strand and a separate antisense strand, wherein:
 - a) each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - b) an 18 to 27 nucleotide sequence of the antisense strand of said nucleic acid molecule is complementary to a human cholinergic receptor muscarinic 3 (CHRM3) RNA sequence comprising SEQ ID NO:305;
 - c) an 18 to 27 nucleotide sequence of the sense strand of said nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human CHRM3 RNA sequence;
 - d) the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends;
 - e) one or more of the nucleotides present in the sense strand, ~~and one or more of the nucleotides present in~~ the antisense strand, ~~or both the sense strand and antisense strand,~~ are 2'-O-methyl modified nucleotides; and
 - f) one to ten or more of the pyrimidine nucleotides present in the sense strand and one to ten or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
43. (Previously Presented) A composition comprising the nucleic acid molecule of claim 42 in a pharmaceutically acceptable carrier or diluent.
44. (Currently amended) A chemically modified nucleic acid molecule, wherein:
 - a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;

- b) each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - c) an 18 to 27 nucleotide sequence of the antisense strand of the nucleic acid molecule is complementary to a human cholinergic receptor muscarinic 3 (CHRM3) RNA sequence comprising SEQ ID NO:305;
 - d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human CHRM3 RNA sequence;
 - e) at least 35 ~~50~~% of the nucleotides of each strand of said nucleic acid molecule comprise modified nucleotides having a ~~sugar~~ modification selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications;
 - f) at least one of said ~~sugar~~ modifications is a 2'-O-methyl modification; and
 - g) ~~each strand of said nucleic acid molecule has no more than 3 consecutive ribonucleotides at least two of said modifications are different from each other.~~
45. (Previously Presented) A composition comprising the nucleic acid molecule of claim 44 in a pharmaceutically acceptable carrier or diluent.
46. (Canceled)
47. (Canceled)
48. (New) The nucleic acid molecule of claim 1, wherein any of the purine nucleotides are 2'-O-methyl purine nucleotides and any of the pyrimidine nucleotides are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
49. (New) The nucleic acid molecule of claim 1, wherein the nucleotides are chemically modified with 2'-deoxy-2'-fluoro, 2'-O-methyl, or 2'-deoxy modifications.